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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/048,033	11/27/2002	H. Michael Shepard	NB 2006.01; 060925-0601	2767

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EXAMINER	
CRANE, LAWRENCE E	
ART UNIT	PAPER NUMBER
1623	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/048,033	SHEPARD, H. MICHAEL	
	Examiner	Art Unit	
	L. E. Crane	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *January 12, 2007 (RCE & amendment)*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17,19-21 and 26-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17,19-21 and 26-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 November 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *01/12/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The sequence listing submitted by applicant has been received, found acceptable, and entered into the USPTO sequence database.

No additional claims have been cancelled, claims **19, 20, 21, 26, 28, 29, 31, 32 and 34-35** have been amended, the disclosure has not been further amended, and new claim **36** has been added as per the amendment filed January 12, 2007. One additional Information Disclosure Statement (1 IDS) has been received with all cited references and made of record. a

Claims **17, 19-21 and 26-36** remain in the case.

Claims **20, 21, 34 and 35** are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims now recite the term "assaying for cell death" (see claim **20** at lines 10-11, but do not further specify the details of any assay. The instant disclosure makes reference to liquid chromatography/mass spectrometry (LC/MS) in a single short paragraph bridging pages 56 and 57 but fails to provide adequate detailed guidance therein to disclose to one of ordinary skill how this analytical tool can be used to execute the method of claims **20, 21, 34 and 35**. Examiner has found no further reference to LC/MS or its application to the analysis method of the instant claims in the remainder of the disclosure. Similarly fluorescence detection is briefly mentioned at page 56, lines 15-19, of the disclosure, but the specifics of its application to achieve the method of claims **20, 21, 34 and 35** do not appear to have been provided therein or elsewhere within the disclosure. Based on these observations examiner believes there is a serious question as to whether the method of claims **20, 21, 34 and 35** was actually in the possession of the instant applicant as of the instant date of filing.

Applicant's arguments filed January 12, 2007 have been fully considered but they are not persuasive.

Examiner notes applicant explanation and respectfully requests applicant to either provide prior art references to support the explanation or note what references presently of record do so, so that examiner can become more familiar with the particulars of the technology

applicant has described. Until this request has been fulfilled examiner shall maintained the rejection.

Examiner notes applicant's amendments, but does not find the amendments to have provided by their entry answers to the questions raised in the previous Office action.; Examiner suggests respectfully that the instant disclosure does not provide sufficient evidence of possession (e.g. the guidance of a working example is not present) and therefore that cancellation would be appropriate.

Claims **17, 19, 26-33 and 36** are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabled for NB1011 in the treatment of a few specific neoplastic disease conditions, does not reasonably provide enablement for the vast array of neoplastic diseases encompassed by either claim **26** or claim **29** or the treatment of any disease condition with multiple active ingredients as specified generically in claim **29** and specifically in claim **17**. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The fundamental issue here is whether practicing the full scope of the instant invention is possible without undue experimentation. As provided for in *In re Wands* (858 F.2d 731, 737; 8 USPQ 2d 1400, 1404 (Fed Cir. 1988) the minimum factors to be considered in determination of whether a conclusion of "undue experimentation" is appropriate are as follows:

A. The breadth of the claims: The claims (**26 and 29**) are directed to the treatment of a large array of disease conditions with a truly vast array of compounds, wherein all but one of proposed active ingredients have not been shown to have the claimed activity. In addition, there has been no showing that multiple active ingredients are effective or, if they are effective, how they are to be administered.

B. The nature of the invention: The invention is directed to the treatment of a wide variety of neoplastic diseases by the administration of compound NB1011 and analogues thereof alone or in combination with other compounds allegedly effective in combination therewith.

C. The state of the prior art: Aside from applicant's own work, there is no prior art which reads on the instant claims.

D. The level of one or ordinary skill: The level skill of the ordinary practitioner is very high in re administration of NB1011, but much lower when other active ingredients are at issue and very much lower when multiple active ingredients are specified in a method of treating a neoplastic disease condition.

E. The level of predictability in the art: The art area is predictable in the areas wherein NB1011 has been shown to have anti-neoplastic activity, but in other areas the predictability becomes indeterminate because of the absence of data.

F. The amount of direction provided by the inventor: The applicant has shown data only for the effective administration of NB1011 in a few disease treatments.

G. The existence of working examples: Working examples are limited to the administration of NB1011 alone in the treatment of only a few specific neoplastic disease conditions.

H. The quantity of experimentation needed to make or use the invention based on the content of the disclosure is deemed to be excessive because only a single example (NB1011) and a few diseases effectively treated *in vitro* is an insufficient basis to extrapolate to the very large number of active ingredients and the large number of different disease conditions encompassed by the instant claims. The scope of the claims is excessive and needs to be very substantially narrowed because the small number of enabling exemplifications can not, and do not, adequately support claims of such a broad scope.

Applicant's arguments filed January 12, 2007 have been fully considered but they are not persuasive.

Examiner notes applicant's amendments, but does not find the amendments to have provided by their entry answers to the questions raised in the previous Office action. Examiner suggests respectfully that the instant disclosure does not provide sufficient support for the breadth of the claims are presently in the case and that a substantial narrowing the claims is in order. One example is deemed to be an insufficient basis for the kind of extrapolation

applicant is requesting. More data would be very helpful in establishing the actual metes and bounds of the medicinally enabled subject matter: see *Ex parte Balzarini* (21 USPQ 2d 1892, 1894 (Bd Pat App & Inter, 1992)). This is the third request for applicant to narrow the scope of the claims.

Claims **26, 29, 32 and 36** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim **29** at lines 36-37, the terms "monophosphate" and "phosphoramidate derivative of an amino acid" are insufficiently detailed to permit the ordinary practitioner to know what particular substituents are being described, and are either confusing or incorrect because the named active ingredients in claim **32** suggest that the functional group present is either -- a mono-phosphate diester -- or
-- a phosphate diester with its third valence occupied by a P-N amide linkage to an amino acid --; i.e. the specific embodiments are not clearly included within the scope of the generic claim. See also claim **26** for the same problem.

Applicant's arguments filed January 12, 2007 have been fully considered but they are not persuasive.

Applicant argues in favor of generic verbal descriptions of classes of compounds but has failed to provide claim language defining the particular substituents being claimed. Examiner notes the statutory requirement to "particularly point out" the subject matter being claimed and respectfully requests structural formulae to meet this requirement.

Claim **29** at lines 2-6 defines a method of treating wherein two active ingredients are present, but fails to define the identity or identities of the first active ingredient (another compound(s) that inhibits thymidylate synthase?), thereby rendering the noted claim incompletely defined.

Applicant's arguments filed January 12, 2007 have been fully considered but they are not persuasive.

Examiner notes newly added claim **36**, but finds this addition does not effectively address the rejection noted above. Applicant's argument is a defense of functional descriptions of active ingredients, a view examiner respectfully disagrees with, noting the requirement of the statute to "particularly point out" the claimed invention. Applicant is respectfully requested to define the active ingredient(s) in the claim in order to meet the statutory requirement.

Claims **26 and 29** make reference to administration of a medicinal compound to a "cell," but are missing the term "in a host in need thereof" or the like. Should applicant amend these claims by introduction of this term, then claim **33** would become superfluous and should be cancelled.

Applicant's arguments with respect to claims **17, 19-21 and 26-35** have been considered but are moot in view of the new grounds of rejection. This new grounds of rejection were necessitated by applicant submission of new and amended claims.

In claims **32 and 36** reference is made to "the compound" in claim **29** but claim **29** makes reference to "a compound" in two separate locations and presumably is making reference to two different compounds. A clarification by amendment is respectfully requested.

Applicant's arguments with respect to claims **17, 19-21 and 26-35** have been considered but are moot in view of the new grounds of rejection. This new grounds of rejection were necessitated by applicant submission of new and amended claims.

The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel,* 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam,* 686 F. 2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi,* 759 F.2d 887, 225 USPQ 645 (Fed. Cir 1985); and *In re Goodman,* 29 USPQ 2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. §1.78(d).

Effective January 1, 1994, a registered attorney or agent or record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R. §3.73(b).

Claims **17, 19-21 and 26-36** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***1-12*** of U. S. Patent No. **6,495,553**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of treatment and the alleged active ingredients are directed to substantially overlapping subject matter.

Claims **17, 19-21 and 26-36** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***36-39*** of U. S. Patent No. **6,339,151**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of treatment and the alleged active ingredients are directed to substantially overlapping subject matter.

Claims **17, 19-21 and 26-36** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***1-7*** of U. S. Patent No. **6,245,750**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of treatment and the alleged active ingredients are directed to substantially overlapping subject matter.

Claims **17, 19-21 and 26-36** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***56-84 and 86-89*** of co-pending Application No. **09/782,721** (for the PG Pubs version, see PTO-892 ref. **P1**). Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds and the methods of treatment are overlapping with the instant claimed subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims **17, 19-21 and 26-36** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***15-18, 21-23 and 27-50*** of co-pending Application No. **09/789,226**. Although the conflicting claims are not identical,

they are not patentably distinct from each other because the compounds and the methods of treatment are overlapping with the instant claimed subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims **17, 19-21 and 26-36** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***1-36*** of co-pending Application No. **11/034,036**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds and the methods of treatment are overlapping with the instant claimed subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims **17, 19-21 and 26-36** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***1-18*** of co-pending Application No. **10/051,320** (for the PG PUBS version, see PTO-892 ref. **P3**). Although the conflicting claims are not identical, they are not patentably distinct from each other because the compounds and the methods of treatment are overlapping with the instant claimed subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims **17, 19-21 and 26-36** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***1 and 53-83*** of co-pending Application No. **10/681,418**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the method of treatment and the alleged active ingredients are directed to substantially overlapping subject matter.

Claims **17, 19-21 and 26-36** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims ***1-10*** of U. S. Patent No. **6,683,061** (PTO-892 ref. **AB**). Although the conflicting claims are not identical, they are not

patentably distinct from each other because the compounds and the methods of treatment are overlapping with the instant claimed subject matter.

Applicant's arguments filed January 12, 2007 have been fully considered but they are not persuasive.

Applicant has acknowledged the validity of the instant rejections but has failed thus far to provide the requested terminal disclaimers. Therefore, the instant rejections have been maintained.

One or more of claims **17, 19-21 and 26-36** of this application conflict with claims ***1-33*** of Application No. **10/119,927**, claims ***56-84 and 86-89*** of Application No. **09/782,721**, claims ***1-18*** of co-pending Application No. **10/051,320**, claims ***1 and 53-83*** of co-pending Application No. **10/681,418**, claims ***1-36*** of copending Application No. **11/034,036**, and claims ***15-18, 21-23 and 27-50*** of copending Application No. **09/789,226**. 37 C.F.R. §1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP §822.

Applicant's arguments filed March 30, 2006 have been fully considered but they are not persuasive.

Applicant has not effective addressed any of the above rejections but has requested deferral until allowable subject matter has been indicated. Therefore all of the above double patenting rejections have been maintained.

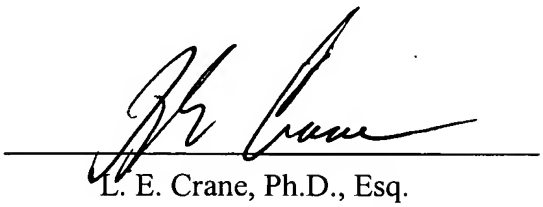
Papers related to this application may be submitted to Group 1600 via facsimile transmission (FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX (unofficially) directly to Examiner's computer is 571-273-0651. The telephone number for sending an Official FAX to the PTO is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. S. Anna Jiang, can be reached at **571-272-0627**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

LECrane:lec
02/20/2007



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